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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,865	08/25/2006	Manuel Sarasa Barrio	105090.61194US	6865

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EXAMINER	
BALLARD, KIMBERLY	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
10/13/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,865	SARASA BARRIO, MANUEL	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-3 and 5-19* is/are pending in the application.

5a) Of the above claim(s) *5 and 8-19* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-3,6 and 7* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1, 6 and 7 have been amended and claim 4 has been canceled as requested in the response filed July 29, 2011. Following the amendment, claims 1-3 and 5-19 are pending in the present application.

2. Claims 5 and 8-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 4, 2009.

3. Claims **1-3, 6** and **7**, drawn to the extent of the peptides of SEQ ID NO: 2 and/or SEQ ID NO: 3, are under examination in the current office action.

Withdrawn Claim Rejections

4. Any objection or rejection of record regarding claim 4 is rendered moot on account of Applicant's cancellation of said claim.

5. The objections to claims 6 and 7 are withdrawn in view of Applicant's amendments to the claims to correct minor typographical mistakes.

6. The rejection of claim 1-3 under 35 U.S.C. 102(e) as being anticipated by US 2006/0188512 by Yednock et al. is withdrawn in view of Applicant's amendments to the claims.

Maintained Claim Rejections

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 6 and 7 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/72880 A2 by Schenk et al. (of record). The rejection is maintained for reasons of record and as discussed below.

Response to Arguments

9. In the response filed July 29, 2011, Applicant argues that with respect to the use of specific Aβ peptides in methods of treating diseases associated with amyloid deposits, Schenk specifies N-terminal Aβ peptides, while the instant SEQ ID NOs: 2 (Aβ33-40) and 3 (Aβ33-42) are from the C-terminal portion of Aβ. According to Applicant, while the Aβ33-42 peptide is used in the examples by Schenk, it was shown not to be effective to reduce amyloid levels in the cortex or hippocampus of transgenic mice when administered as an immunogen. Therefore, Applicant contends that Schenk does not disclose a method of treating humans with disease using the Aβ33-42 or

Aβ33-40 peptides to induce antibodies against Aβ effective to reduce amyloid levels. Further, Applicant argues that administration of the Aβ33-42 peptide to PDAPP transgenic mice does not constitute administration to a "patient" as claimed, because the instant specification describes human subjects as "patients" whereas PDAPP transgenic mice are referred to as "transgenic mice". Thus, Applicant contends, the skilled artisan would understand that "patients" means human subjects and not transgenic mice.

10. Applicant's arguments have been fully considered but they are not persuasive. Contrary to Applicant's assertions, Schenk's teachings are not limited to N-terminal Aβ immunogenic peptides and the peptides illustrated in the Examples, but rather the document's teachings encompass the *entire* disclosure. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied,* 493 U.S. 975 (1989). See also >*Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005). Accordingly, it does not matter whether or not the C-terminal Ab peptides, such as the Aβ33-42 peptide, are preferred embodiments of the Schenk document, because this peptide is taught by Schenk to be useful in the treatment of subjects having a disease associated with amyloid deposits in the brain, such as Alzheimer's disease, and thus are anticipatory for the instantly recited invention. As further evidence that the C-terminal fragment Aβ33-42 was actually considered useful by Schenk, it is noted that US Patent No. 6,905,686 to Schenk, which is related to the

instant WO document in that they both have the same priority documents and nearly-identical disclosures, has claims directed to a method for treating Alzheimer's disease in a subject comprising administering an immunogenic fragment of Aβ in a regime effective to produce an immune response comprising antibodies against Aβ, wherein the Aβ fragment is Aβ33-42, and wherein the subject is a human (see claims 24, 35 and 46). Because U.S. patented claims are presumed to be enabled, the disclosed subject matter encompassing the use of the Aβ33-42 peptide for immunotherapy in Alzheimer's disease patients according to the present WO document, based on its relationship with the '686 patent, would therefore also be presumed enabled and would thus be expected to elicit an appropriate immune response comprising antibodies that specifically recognize Aβ42 peptide and reduce amyloid deposition upon immunization of a patient with the Aβ33-42 peptide. Note that the use of the '686 patent here is to evidence the enablement of the WO document's teachings, particularly in response to the presently amended claims.

And regarding Applicant's arguments about the use of the term "patient", Schenk clearly states that the term "patient" includes human and other mammalian subjects that receive either prophylactic or therapeutic treatment (see p. 11, lines 24-25). Regardless, it is noted that the features upon which applicant relies (i.e., that the term "patients" only refers to human subjects) are not recited in the rejected claim(s). That is, the instant claims do not actually recite that the "patient" is a human. Although the claims are interpreted in light of the specification, limitations from the specification are

not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the rejection of claims 1-3, 6 and 7 is maintained.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-3, 6 and 7 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0073655 A1 by Chain (of record). The rejection is maintained for reasons of record and as discussed below.

Response to Arguments

13. In the response filed July 29, 2011, Applicant argues that Chain does not provide a reasonable expectation of successfully treating an amyloidogenic disease comprising administering an effective amount of the peptides recited in the present claims. Applicant asserts that Chain does not exemplify antibodies produced using or specific for the peptides of instant SEQ ID NO: 2 or 3, and therefore even if Chain did make obvious active immunization, Chain does not provide a reasonable expectation of success for active immunization with the recited peptides.

Applicant further argues that the other references provided in the Office action, i.e., Schenk and Yednock, teach away from Applicant's claimed invention. For example, Applicant contends that Schenk's teachings on the 21F12 and 16C11 antibodies, which have specificity for an epitope within Aβ33-42 and which were found not to bind or clear amyloid deposits, constitutes a teaching away from the presently claimed invention. According to Applicant, the teachings away in Schenk provide further support for the fact that disclosure of passive immunization with Aβ peptides does not provide any reasonable expectation that the use of Aβ peptides not tested in Chain would be successful.

14. Applicant's arguments have been fully considered but they are not persuasive. It is noted that the instant rejection is based upon the Chain reference alone, and not

Chain in view of either the Schenk or Yednock references of record. While the examiner alluded to the teachings of these references, it was only to exemplify the general knowledge in the art at the time of filing, that is, that both active immunization (administration of immunogenic Aβ peptides) and passive immunization (administration of anti-Aβ antibodies) techniques were known as the two main immunotherapeutic approaches in the treatment of Alzheimer's disease.

Because the Schenk document is not relied upon as an integral reference in this rejection, it cannot constitute a "teaching away" as Applicant insists. The fact remains that Chain explicitly teaches that antibodies directed to amino acids 33-40 of Aβ (or residues 33-42 of Aβ) are useful for therapy, such as in the treatment of Alzheimer's disease (see [0076]). Chain also teaches methods for the production of such antibodies, which include conjugating the Aβ peptides to a protein carrier, such as KLH, wherein Chain teaches that a cysteine residue can be added to the end of the immunogenic peptides in order to facilitate coupling to the carrier protein (see [0080]). Chain also teaches that humans are suitable hosts for the production of antibodies (see [0082]). Accordingly, Chain expressly teaches the administration of an Aβ33-40 or Aβ33-42 peptide conjugate to a human patient in order to produce antibodies directed against Ab peptide, wherein such antibodies are therapeutically useful for the treatment of Alzheimer's disease. Hence, it would have been obvious to one of ordinary skill in the art to simply administer the immunogenic composition comprising the KLH-conjugated Aβ33-40 or Aβ33-42 peptide to a patient in order to treat Alzheimer's

disease instead of producing human (or humanized) antibodies first and then administer the antibodies to the patient, as taught by Chain.

Furthermore, if Schenk is to be relied upon (as Applicant insists) for teaching whether or not the ordinarily skilled artisan would have had a reasonable expectation of success, one should look to directly analogous molecules (i.e., immunogenic Aβ peptides rather than specific monoclonal anti-Aβ antibodies) to determine the relative effectiveness of a given therapeutic method. It is again noted that U.S. Patent No. 6,905,686 (filed Nov. 28, 2000; noted above) by Schenk has claims directed to a method of treating Alzheimer's disease in a human subject, comprising administering an effective dose of Aβ33-42 peptide to produce antibodies against Aβ (see claims 24, 35 and 46). Because patented claims are presumed enabled, such claims would evidence the suitability of these peptide epitopes for therapeutic purposes, which would have provided the ordinary artisan with a reasonable expectation that a peptide directed to the C-terminus of Aβ, such as Aβ33-40 or Aβ33-42, could be successfully used therapeutically. Again it is noted that the use of the '686 patent in this discussion was necessitated by Applicant's arguments and claim amendments, but does not in fact change the basis of the rejection. Accordingly, the rejection of claims 1-3, 6 and 7 is maintained.

Conclusion

15. No claims are allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is (571)272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Kolker can be reached on 571-272-3181. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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